## REMARKS

Claims 20, 28, 30, 32, 33, 35 and 39-42 are pending in the application. Claims 20, 28, 30, 32, 33, 35 and 39-42 stand rejected. Claims 20, 35 and 39 have been amended. New claims 43-48 have been added.

Support for the amendments to the claims and for new claims 43-48 can be found throughout the application as originally filed. Support for the hybridization language in new claims 45-48 can be found, *inter alia*, in paragraph [0058]. Paragraph numbering is as set forth in U.S. published patent application 20040219528.

No new matter has been added.

Upon entry of this amendment, claims 20, 28, 30, 32, 33, 35 and 39-48 will be pending.

### Withdrawn Rejections

Applicants thank the Office for the indication that the following rejections were withdrawn:

1) Rejection of claim 35 under 35 U. S. C. § 112, second paragraph;

2) Rejection of claims 21 and 24 under 35 U. S. C. § 112, first paragraph (written description);

3) Rejection of claims 20-24 under 35 U. S. C. § 102(e) over U.S. Patent 6,812,339 (Venter); and

4) Rejection of claims 20-26, 29, 30 and 34 under 35 U. S. C. § 102(b) over Yamamoto *et al.* (Leukemia, 13:595-600, 1999).

### Rejections under 35 U. S. C. § 112, first paragraph (enablement)

Claims 20, 28, 30, 32, 33, 35 and 39-42 remain rejected under 35 U. S. C. § 112, first paragraph, for an alleged lack of enablement. The Office alleges that "the specification, while being enabling for methods of diagnosis of colon cancer comprising the differential detection of PPP3CC protein levels, does not reasonably provide enablement for methods for diagnosing colon cancer, lymphoma, stomach cancer, prostate cancer, breast cancer or carcinoma,

comprising either the differential detection of PPP3CC mRNA levels, where the PPP3CC mRNA is defined as a nucleotide sequence of SEQ ID NO:1587 or a sequence at least 98% identical to SEQ ID NO:1587..." (Office Action, page 3). Applicants respectfully disagree.

Preliminarily, Applicants note that claims 20, 35 and 39 have been amended. Claims 20 and 39 were amended to include a function/activity while claim 35 was amended to identify specific cancers.

Applicants respectfully submit that given the level of skill in the art, the state of the art, and the teachings of the specification, one of ordinary skill in the art would be able to practice the presently claimed methods without any undue experimentation. The Examiner has acknowledged that the application enables diagnosing colon cancer based on differential detection of PPP3CC protein levels. However, notwithstanding the Office's brief reference to references cited by the Office and discussed in Applicants' previous response, the Office has failed to identify what is lacking in the present specification or in the knowledge of the person of ordinary skill in the art to allow such a person to practice the claimed invention by comparing levels of mRNA sequences to diagnose cancer. Further, the Office failed to specifically identify any disclosure in Lakshmikuttyamma stating why one could not "extrapolate from the data in Lakshmikuttyamma [based on protein levels] to a method where the diagnosis is based on observations of mRNA levels".

The Office also alleges that there is "no association between differential calcineurin (PPP3CC) mRNA expression and colon cancer, prostate cancer, lymphoma, breast cancer, or broadly 'carcinoma' ", noting that teachings referred to by Applicant "are prophetic". Applicants do not agree.

Applicants note that the association between PPP3CC and cancer is set forth in the specification as filed which identifies PPP3CC as a carcinoma associated gene or "CA sequence" (paragraph [0023] and Table 108). The specification also recites that altered expression of the CA sequence is indicative of specific cancers (see, *inter alia*, paragraphs [0023] and [0028]). The specification recites that "CA sequences are those that are up-regulated in carcinomas; that is, the expression of these genes is higher in carcinoma tissue as compared to normal tissue of the same differentiation stage." (paragraph [0037]).

The fact that the specific endpoints claimed by Applicants, for example, may not be part of a working example in the specification appears irrelevant to enablement. Even though data showing these endpoints (up-regulation of at least 50%, at least 100%, or at least 150%, compared to a control) may not have been specifically set forth in a working example in the application as filed, there is no requirement for this information to be in a working example. Indeed, it is established law that there is no requirement for a "working" example if the disclosure is such that one skilled in the art can practice the claimed invention. *In re Borkowski*, 164 U.S.P.Q. 642 (C.C.P.A. 1970); *Ex parte Nardi*, 229 U.S.P.Q. 79 (Pat. Off. Bd. App. 1986). Since, as disclosed above, there is no reason to believe that one skilled in the art would not be able to practice the claimed inventions, there is no requirement for a working example providing these endpoints.

Applicants further point out that the lack of predictability said by the Office to be provided in the Tockman reference is tempered by a subsequent Tockman publication which is inconsistent with the Office's position. In the subsequent Tockman study, Tockman *et al.* (Tockman et al., Clin. Can. Res. 3:2237-2246, 1997) demonstrate the diagnostic efficacy of an *in vitro* assay for the up-regulation of a single gene (hnRNP A2/B1) for certain populations at risk for developing lung cancer . Overexpression of hnRNP A2/B1 predicted development of primary lung cancer with an overall accuracy of **73%**, which represented a **3-fold increase** in diagnostic sensitivity over the routine detection method; see Tockman *et al.* (1997) at page 2242 (emphasis added). The Tockman *et al.* (1997) reference also stated that "[r]eplicated but preliminary prospective observations support the promise of hnRNP A2/B1 as a lung cancer diagnostic." (Tockman *et al.* (1997) at page 2244). Tockman *et al.* also expressed confidence that "for populations at this level of risk, using sputum cells to monitor hnRNP A2/B1 expression may greatly improve the accuracy of preclinical lung cancer detection." (Tockman *et al.* (1997) at page 2244). After noting the diagnostic efficacy of their *in vitro* assay, Tockman *et al.* noted that "conclusive determination of hnRNP A2/B1 predictive value (and demonstration of associated lung cancer mortality reduction of at least 50%) in a general population of current and former smokers ... must await a prospective intervention trial of more than 10,000 participants

similar to the multicenter National Cancer Institute collaboration." (Tockman *et al.* (1997) at page 2244).

Applicants respectfully assert that the Tockman *et al.* (1997) reference (as well as the Tockman *et al.* (1992) reference cited by the Office) provides evidence that those having ordinary skill in the art were able to express confidence in the diagnostic ability of disease markers even in the absence of results from full-blown clinical trials. One having ordinary skill in the art, upon reading either Tockman reference, would certainly not construe Tockman *et al.* as suggesting that, in the absence of irrefutable clinical trial evidence, their results were somehow ambiguous, unpredictable, uncertain, flawed, or unreliable. Applicants submit that the standard for enablement is not a "certainty" of success, but a "reasonable expectation" of success, and that a "conclusive determination" or "irrefutable" demonstration of diagnostic efficacy is not required for patentability. The courts have consistently held that this is not the proper level of inquiry when assessing utility and enablement under Title 35. The proper standard for enablement is that the specification teach those of ordinary skill in the art how to make and use the invention without "undue experimentation." MPEP 2164.01.

Applicants respectfully submit, that in this case, the specification describes the identification of SEQ ID NO:1587 as a diagnostic indicator of specific cancers as well as how to use the carcinoma associated sequence in, *inter alia*, the diagnosis of cancer. Thus, Applicants respectfully submit that a skilled artisan would readily be able to make and use the invention defined by the pending claims, based on the disclosure in the application. Accordingly, Applicants respectfully request that the rejection of claims 20, 28, 30, 32, 33, 35 and 39-42 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Thus, based on the above remarks, Applicants submit that the claims are enabled under 35 U.S.C. §112, first paragraph.

**Rejections under 35 U. S. C. § 112, first paragraph (written description)**

Claims 20, 28, 30, 32, 33 and 39-42 were rejected under 35 U. S. C. § 112, first paragraph, for an alleged lack of written description support. The Office asserted that "the

specification fails to describe the genus of mRNA expression products of PPP3CC that have greater than 98% sequence identity to SEQ ID NO:1587 and that are also diagnostic of cancer or diagnostic for a specific cancer." Because one of skill in the art would readily appreciate that the inventors had possession of the claimed invention at the time the present application was filed, Applicants respectfully traverse.

Preliminarily, Applicants point out that claims 20, 28, 30, 32, 33 and 39-42 are directed to specific cancers, e.g. to methods for diagnosing either colon cancer or carcinoma, lymphoma, prostate cancer, stomach cancer and breast cancer, not, as the Office appears to suggest ("diagnostic of ***cancer*** or diagnostic for a specific cancer"; emphasis added), to ***any*** cancer. Also, as amended, claims 20 and 39 (as well as the claims depending from claims 20 and 39) recite that the expression product encodes a polypeptide with protein phosphatase activity.

Applicants respectfully point out that it appears that claim 28 was erroneously included in the present rejection. Claim 28 does not recite a genus of sequences, instead reciting that "the expression product is a mRNA having a sequence of SEQ ID NO:1587".

The specification provides sufficient written description for the pending claims as evidenced by the U.S. Patent and Trademark Office's own guidelines on the subject: Synopsis of Application of Written Description Guidelines, www.uspto.gov/web/menu/written.pdf ("Guidelines"). Example 14 of the Guidelines illustrates a hypothetical situation that mirrors the present case. Example 14 provides an example of a product by function claim, where the specification teaches that SEQ ID NO:3 and "variants that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" are essential to the operation of the claimed invention. Example 14 then provides the following guidance to examiners:

> The specification indicates that the genus of [nucleic acids] that must be variants of SEQ ID NO:3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified [kinase-encoding] activity. One of skill in

> the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
> Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

As in the Example 14 hypothetical, the present claims are drawn to a genus of molecules whose "variants must possess the specified activity and must have identity to" a reference sequence. In claims 20, 28, 30, 32, 33 and 39-42, polynucleotide expression products have at least 98% sequence identity to SEQ ID NO:1587. Applicants reiterate that the minimum level of sequence identity in claims 20, 28, 30, 32, 33 and 39-42 is at least 98%, a level ***far*** above the level of identity recited in Example 14 of the Guidelines, thereby further increasing the required similarity between members of the genus. The present application discloses the species SEQ ID NO:1587 and information relating to variants. Pending claims 20 and 39, and the claims depending from claims 20 and 39 recite that the expression product encodes a polypeptide with protein phosphatase activity.

In *Ex parte Sun* (Appeal No. 2003-1993; copy enclosed), the Board of Patent Appeals and Interferences considered the appropriateness of rejections under the written description and enablement requirements where the specification discloses a molecule within the claims and a functional assay for activity. The Board explained in *Ex parte Sun* that the following claim was illustrative of those on appeal.

> 31. An isolated wee1 nucleic acid molecule comprising a member selected from the group consisting of:
> (a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2;
> (b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;
> (c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
> (d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The specification of the application on appeal disclosed that SEQ ID NO:2 encoded a protein having a defined function (similar to that of a known tyrosine kinase). The specification

explained that the protein is useful in genetic engineering of corn plants to increase productivity. The examiner had rejected claim 31 as failing to meet the written description requirement, arguing that one skilled in the art could not predict the structure and function of nucleic acid "comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" The examiner had also argued that the specification did not "teach a single representative species with 80% identity and WEE1 function".

After reviewing the relevant case law, including *Lilly* and *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002), the Board concluded that the rejected claims, including claim 31, met the written description requirement. The Board pointed out that the specification describes the sequence of a nucleic acid molecule encoding SEQ ID NO:2 and the sequence of a nucleic acid molecule comprising the coding sequence of SEQ ID NO:1. The Board also noted that the specification provides a description how to screen for WEE1 activity. The Board concluded that,

> [I]t would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with *Enzo*.
> In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

In the present case, as in *Ex parte Sun*, a functional limitation is provided. One of skill in the art at the time the present application was filed would be able to determine whether sequences falling within the claimed genus satisfied the functional limitation, e.g. whether encoded polypeptides have protein phosphatase activity. In *Ex parte Sun* the Board further concluded that the written description requirement was met even though only a single species is disclosed.

Accordingly, it is clear that the disclosure of even a *single* species combined with a functional assay provides an adequate written description for a claim to a genus of molecules.

A person skilled in the art would recognize, upon reading the disclosure, that Applicants invented the claimed subject matter, including 98% homologs sharing structural features with the specifically claimed and disclosed sequences.

Claim 42 was rejected under 35 U. S. C. § 112, first paragraph, for an alleged lack of written description support. The Office alleges that there is no support for the limitation in claim 42 that the "expression product at least 98% identical to SEQ ID NO:1587 has the same expression profile as SEQ ID NO:1587." Because the specification discloses the limitation, Applicants respectfully disagree.

Paragraph [0023] sets forth that "the present invention provides nucleic acid and protein sequences that are associated with carcinoma, herein termed 'carcinoma associated' or 'CA" sequences. Further, the specification states in paragraph [0028] that altered CA sequences can show the "same expression profile" as the CA sequences. Paragraph [0147] provides further written description support for the cited limitation, albeit in screening methodologies, stating that effect of candidate agents will be analyzed "where the CA sequence has been altered but shows the same expression profile ...".

Applicants respectfully submit that the new claims added herein are also supported by adequate written description and are consistent with the Written Description Guidelines. Example 10 provides an example of a process claim, where the specification teaches that SEQ ID NO:10 and "any DNA which hybridizes under specified stringent conditions to SEQ ID NO: 10 will be useful as a marker for detecting the presence of Burkitt's lymphoma." Claim 1 of Example 10 reads "[a] process for producing an isolated polynucleotide comprising hybridizing SEQ ID NO: 10 to genomic DNA in 6XSSC and 65°C..." (see page 38 of the Guidelines). As stated in the analysis of claim 1

> ... the essential feature of the claimed invention is a process of obtaining a nucleic acid sequence which is identified by a probe that hybridizes to SEQ ID NO:10 and a polynucleotide that hybridizes with SEQ ID NO: 10. ... The claim is drawn to a genus ... The specification presents an example where a single species has been reduced to practice ... Therefore the disclosed

> species within the genus has been adequately described. Now turning to the genus analysis, the art indicates that there is no substantial variation within the genus because of the stringency of hybridization conditions which yields structurally similar molecules. The single disclosed species is representative of the genus because reduction to practice of this species, considered along with the defined hybridization conditions and the level of skill and knowledge in the art, are sufficient to allow the skilled artisan to recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus. ... Claim 1 is adequately described"

(see pages 38 to 40 of the Synopsis of Application of Written Description Guidelines). Consistent with the analysis above, in the instant application, the essential feature of new claims 45-48 is that a nucleic acid that hybridizes to SEQ ID NO:1587 under defined hybridization conditions and is useful for diagnosing prostate cancer, stomach cancer and breast cancer.

Applicants respectfully assert that one skilled in the art would appreciate that the applicant was in possession of the claimed invention at the time the present application was filed. Accordingly, Applicants respectfully request the withdrawal of this rejection upon reconsideration.

## CONCLUSION

The foregoing represents a bona fide attempt to advance the present application to allowance. Applicants respectfully assert that all claims are in condition for allowance, which action is hereby requested. The Examiner is invited to telephone the undersigned attorney at (302) 778-8458 if such would expedite prosecution.

No fee is believed due for the filing of Applicants' Response to Office Action. Please apply the fee for the filing of the Request for Continued Examination and any other charges or credits to deposit account 06-1050 referencing Attorney Docket No. 20366-027001.

Respectfully submitted,

Date: **October 26, 2007**

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# UNITED STATES PATENT AND TRADEMARK OFFICE

## BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993
Application No. 09/470,526

ON BRIEF

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

## DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the

coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613 .

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including

those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1

polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant

whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote

omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

## CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

| | |
|---|---|
| WILLIAM F. SMITH<br>Administrative Patent Judge | ) |
| DEMETRA J. MILLS<br>Administrative Patent Judge | ) APPEALS AND |
| | ) INTERFERENCES |
| ERIC GRIMES<br>Administrative Patent Judge | ) |

Appeal No. 2003-1993
Application No. 09/470,526

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